EDWARD R. REINES (Bar No. 135960)
edward.reines@weil.com
DEREK C. WALTER (Bar No. 246322)
derek.walter@weil.com
NATE NGEREBARA (Bar No. 317373)
nate.ngerebara@weil.com
MELINDA ROOT (Bar No. 334485)
melinda.root@weil.com
WEIL, GOTSHAL & MANGES LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
Telephone: (650) 802-3000
Facsimile: (650) 802-3100

ANDREW P. GESIOR (*pro hac vice*)
andrew.gesior@weil.com
WEIL, GOTSHAL & MANGES LLP
767 Fifth Avenue
New York, NY 10153
Telephone: (212) 310-8000
Facsimile: (212) 310-8007

DOUGLAS W. MCCLELLAN (*pro hac vice*)
doug.mcclellan@weil.com
MELISSA L. HOTZE (*pro hac vice*)
melissa.hotze@weil.com
WEIL, GOTSHAL & MANGES LLP
700 Louisiana, Ste. 1700
Houston, TX 77002
Telephone: (713) 546-5000
Facsimile: (713) 224-9511

AUDRA SAWYER (Bar No. 324684)
audra.sawyer@weil.com
WEIL, GOTSHAL & MANGES LLP
2001 M Street NW, Suite 600
Washington, DC 20036
Telephone: (202) 682-7274

Attorneys for Plaintiffs,
ILLUMINA, INC. AND
ILLUMINA CAMBRIDGE LTD.

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

ILLUMINA, INC. and
ILLUMINA CAMBRIDGE LTD.,

Plaintiffs,

v.

BGI GENOMICS CO., LTD.,
BGI AMERICAS CORP.,
MGI TECH CO., LTD.,
MGI AMERICAS, INC., and
COMPLETE GENOMICS INC.,

Defendants.

COMPLETE GENOMICS INC.,

Counterclaim-Plaintiff,

v.

ILLUMINA, INC., and
ILLUMINA CAMBRIDGE LTD.,

Counterclaim-Defendants.

Case No. 3:19-cv-03770-WHO
Case No. 3:20-cv-01465-WHO

PLAINTIFFS' NOTICE OF MOTION AND MOTION FOR JUDGMENT AS A MATTER OF LAW – REBUTTAL CASE

Judge William H. Orrick

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

NOTICE OF MOTION

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that as soon as the Court may practically hear before the Honorable William H. Orrick, United States District Court, Northern District of California, 450 Golden Gate Ave., Courtroom 2, San Francisco, CA 94102, plaintiffs Illumina, Inc. and Illumina Cambridge LTD. (collectively "Illumina"), will and hereby does move for judgment as a matter of law that Defendants Complete Genomics, Inc., BGI Genomics Co. Ltd., BGI Americas Corp., MGI Tech Co., Ltd., and MGI Americas, Inc. (collectively "BGI") have failed to meet their burden to prove that U.S. Patent No. 7,566,537 (the "'537 Patent"), U.S. Patent No. 9,410,200 (the "'200 Patent"), U.S. Patent No. 10,480,025 ("the '025 Patent"), U.S. Patent No. 7,771,973 (the "'973 Patent"), and U.S. Patent No. 7,541,444 ("the '444 Patent") (collectively, the "Asserted Patents") are invalid on any basis, including obviousness under 35 U.S.C. § 103, lack of enablement under 35 U.S.C. § 112, and lack of written description under 35 U.S.C. § 112.

This motion is based on this notice and supporting memorandum, the trial record, and such other matters of which the Court may take judicial notice.

RELIEF REQUESTED

Illumina respectfully seeks an order that the Asserted Patents are not invalid.

MEMORANDUM OF POINTS AND AUTHORITIES

I. INTRODUCTION

On June 15, 2021, this Court, in granting Illumina's Motion for Preliminary Injunctions, found that "BGI has failed to satisfy its burden of showing by clear and convincing evidence that the '973 patent is invalid for lack of enablement" and "BGI has not demonstrated a substantial question as to the invalidity of Illumina's patents with respect to obviousness" because "BGI has not adequately established that a POSITA would have been motivated to combine Parce and Zavgorodny (or both Zavgorodny references) or that a POSITA would expect a reasonable likelihood of success" and "a closer look at BGI's arguments confirms that the current obviousness argument is akin to those that have already been rejected by prior courts and the IPR Board." Dkt. No.[1] 185 at 12-13, 15-17. On August 27, 2021 this Court denied BGI's Motion for Summary Judgment that the '973 Patent is invalid for failure to satisfy the enablement and written description requirements under 35 U.S.C. § 112. 1465 Dkt. No. 469 at 1, 11. On September 9, 2021, this Court granted Illumina's Motion for Summary Judgment that "the '444 Patent is not invalid for lack of written description or enablement" and "the Asserted Claims are not anticipated." Dkt. No. 424 at 25. Illumina hereby moves for judgement as a matter of law ("JMOL") on the following issues:

- BGI has failed to meet its burden of proving by clear and convincing evidence that claims 1, 4, and 6 of the '537 Patent, claims 11 and 19 of the '200 Patent, claims 1, 9, 27, 31, 33, 34, 42, 47, and 50 of the '025 Patent, claim 13 of the '973 Patent, and claim 3 of the '444 Patent (collectively the "Asserted Claims") are invalid as obvious under 35 U.S.C. § 103;
- BGI has failed to meet its burden of proving by clear and convincing evidence that the Asserted Claims are invalid for lack of enablement under 35 U.S.C. § 112; and
- BGI has failed to meet its burden of proving by clear and convincing evidence that the Asserted Claims are invalid for lack of written description under 35 U.S.C. § 112.

[1] All citations to the docket refer to the docket in Case No. 3:19-cv-03770-WHO, unless otherwise specified.

This memorandum highlights key reasons why JMOL is warranted. There are additional reasons and evidence set forth throughout the record that support this motion. Plaintiffs are therefore entitled to judgment as a matter of law that none of the Asserted Claims are invalid.

II. BACKGROUND

Illumina's patent rights to its azido chemistry are valid and battle-tested. BGI's invalidity positions are just another attempt to revive arguments that have been repeatedly rejected by this Court, the PTAB, and the Federal Circuit. In 2016, another multi-national life-sciences company, Qiagen N.V., attempted to introduce sequencers using Illumina's patented azido chemistry. *See* TX1783 at 001-002. Before doing so, it attempted to challenge the '537 Patent before the PTAB. *See* TX1803. The PTAB upheld Illumina's patent after a trial. *Id*. Qiagen appealed to the Federal Circuit, which also upheld Illumina's patent. TX0413. In doing so, the Federal Circuit relied on the PTAB's finding that the use of an azidomethyl protecting group for SBS would have been non-obvious to a person of ordinary skill in the art. *Id.* at 015 ("[A] person of ordinary skill in this field would not have been motivated to use the azidomethyl group of Zavgorodny as a 'protecting group [that] can be modified or removed to expose a 3′ [hydroxyl] group' of a nucleic acid molecule, as the claim requires. This is so because the azidomethyl group would have been expected to perform inefficiently in that role.").

Although its validity challenges failed before the PTAB, Qiagen attempted to nevertheless introduce its infringing sequencers into the United States. TX1783 at 001-002. In doing so, it attempted to argue that there were still substantial questions as to the validity of Illumina's '537 patent. This included three theories that the patent was invalid for lack of enablement set forth by Dr. Metzker, who was Qiagen's expert during the preliminary injunction proceedings. Trial Tr.[2] at 870:9-12; 875:10-876:11. However, Judge Alsup thoroughly rejected Qiagen's invalidity arguments, including its three enablement arguments, and found that it is likely the validity of Illumina's patent rights will be upheld. TX1783; Trial Tr. 876:13-877:21. Because of the strength of Illumina's azido patent rights, Judge Alsup found that Illumina presented a "powerful" case for an injunction. *Id.* at 016.

In 2017, Defendants invested in two IPRs trying to challenge the '537 Patent despite Qiagen's

[2] References to Trial Tr. refer to the trial transcripts in this case from November 15-19, 2021. *See* Dkt. Nos. 512, 515, 519, 523, 524.

previous failures. *See* TX984; TX985. As part of those proceedings, BGI submitted 60 prior art references to the PTAB. Trial Tr. 1022:16-19. The PTAB rejected Defendants' challenges because one was duplicative of Qiagen's prior failed IPR and their second IPR failed to show a reasonable likelihood on the merits that the '537 Patent was invalid. *See* TX986; TX987; *see also* Trial Tr. at 1022:5-15 (BGI's IPR challenges were "substantially basically identical" to Qiagen's challenges).

Illumina's expert, Dr. Floyd Romesberg, testified that the history of these prior challenges were directly relevant to BGI's invalidly arguments here. *See* Trial Tr. 1020:9-21. Although the prior challenges were focused on the '573 patent, the reasoning of the 10 judges who previously reviewed that patent applies to all of the asserted patents in the case. Trial. Tr. at 1020:9-1021:7. This is because all of the patents-in-suit "claim the azidomethyl nucleotide invention, and so the judges' opinion about those would be the same in each patent." *Id.* at 1021:8-15.

III. LEGAL STANDARD

A. Judgment As A Matter Of Law

Pursuant to Rule 50(a), a court may grant judgement as a matter of law "[i]f a party has been fully heard on an issue during a jury trial and the court finds that a reasonable jury would not have a legally sufficient evidentiary basis to find for the party on that issue." Fed. R. Civ. P. 50(a). "The grant or denial of a motion for judgment as a matter of law is a procedural issue not unique to patent law, reviewed under the law of the regional circuit in which the appeal from the district court would usually lie." *Summit Tech., Inc. v. Nidek Co., Ltd.*, 363 F.3d 1219, 1223 (Fed. Cir. 2004). In determining whether to grant a motion for judgement as a matter of law, "the Court must draw all reasonable inferences in favor of the nonmoving party, and determine whether reasonable minds could come to a single conclusion in favor of the moving party." *MediaTek Inc. v. Freescale Semiconductor, Inc.*, No. 11-5341, 2014 WL 4643947, at *1 (N.D. Cal. Sept. 17, 2014) (citing *E.E.O.C. v. Go Daddy Software, Inc.*, 581 F.3d 951, 961 (9th Cir. 2009)). "A district court may grant a motion for judgment as a matter of law pursuant to Rule 50(a) or (b) 'when the evidence presented at trial permits only one reasonable conclusion,' *i.e.*, 'if no reasonable juror could find in the non-moving party's favor.'" *Nichols v. City of San Jose*, 2017 WL 3007072, at *1 (quoting *Torres v. City of Los Angeles*, 548 F.3d 1197, 1205 (9th Cir. 2008)) (internal quotation marks and citations omitted).

B. Obviousness

It is well-settled that a party asserting obviousness must set forth evidence that a "skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success." *PAR Pharmaceutical, Inc. v. TWI Pharmaceuticals, Inc.*, 773 F.3d 1186, 1192 (Fed. Cir. 2014); *see also in re Stepan,* 868 F.3d 1342 (Fed. Cir. 2017) ("An obviousness determination requires finding both 'that a skilled artisan would have been motivated to combine the teachings of the prior art . . . and that the skilled artisan would have had a reasonable expectation of success in doing so.'") (citing *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.,* 821 F.3d 1359, 1367-68 (Fed. Cir. 2016)).

C. Enablement

"[W]hether a patent satisfies the enablement requirement is a question of law based on underlying factual findings." *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1096 (Fed. Cir. 2020) (citation omitted). "'To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.' … 'Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations'" such as the *Wands* factors. *Amgen Inc. v. Sanofi, Aventisub LLC*, 987 F.3d 1080, 1084 (Fed. Cir. 2021) (citation omitted). The *Wands* factors are:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). A "patent's specification need not 'describe how to make and use every possible variant of the claimed invention'" so long as it teaches "those skilled in the art how to make and use the full scope of the claimed invention 'without undue experimentation.'" *McRO*, 959 F.3d at 1100 (citations omitted). Further, "'[e]ven if some of the claimed combinations were inoperative, the claims are not necessarily invalid.'" *EMI Grp. N. Am., Inc. v. Cypress Semiconductor Corp.*, 268 F.3d 1342, 1348–49 (Fed. Cir. 2001) (quoting *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.,* 750 F.2d 1569, 1576–77 (Fed.Cir.1984)). To show that some number of inoperative combinations render a claim non-enabled typically requires a showing that "the number of

inoperative combinations" is "significant" or that a POITSA would be required "to experiment unduly in order to practice the claimed invention." *Id*. The enablement "requirement is limited to what is claimed. Section 112 requires enablement of 'only the claimed invention,' not matter outside the claims." *McRO*, 959 F.3d at 1100 (citation omitted). "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997); *McRO*, 959 F.3d at 1100-1102 ("the specification must reasonably teach how to make and use [the novel] aspect of the invention").

D. Written Description

"The issue of whether a claimed invention satisfies the written description requirement is a question of fact." *Centrak, Inc. v. Sonitor Techs., Inc.*, 915 F.3d 1360, 1365 (Fed. Cir. 2019) (citation omitted). The Federal Circuit has "held that the test for sufficiency of a patent's written description is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* The sufficiency of the written description is viewed from the perspective of a person of ordinary skill in the art. *Bos. Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011).

IV. ARGUMENT

The Asserted Patents are entitled to a presumption of validity. *Microsoft Corp. v. I4I Ltd. P'ship*, 564 U.S. 91, 100 (2011). BGI, as the patent challenger, has the burden of establishing invalidity by clear and convincing evidence. *Id.* at 95, 100; *see also* Trial Tr. 865:3-7. BGI has failed to meet its burden of clear and convincing evidence that the patents are invalid.

A. BGI Has Failed To Prove The Asserted Claims Are Invalid As Obvious

The evidence adduced at trial overwhelmingly supports the non-obviousness of the Asserted Patents because, in addition to BGI's failure of proof described below, there is a strong showing of objective indicia of non-obviousness. Examples include the past Patent Office and Court decisions and ample evidence in the record of long-felt but unmet need, failure of others (including BGI's expert witness Dr. Metzker and a Nobel Prize laureate), copying, unexpected results, skepticism, industry praise, and commercial success. All of BGI's obviousness combinations suffer from hindsight and cannot meet the burden of showing that the Asserted Patents would be invalid. Trial Tr. 1050:6-8.

For example, as described above, the '537 Patent has been battle-tested, and the Patent Office has repeatedly found that it would not be obvious to combine Zavgorodny[3] or other references disclosing azidomethyl with any sequencing-by-synthesis ("SBS") method. *See* § II.A.; *see also* Trial Tr. 1022:9-15 (the validity arguments at issue at this trial are with the exception of "a few small changes of substituting in the sequence by synthesis reference for another, they're basically the same thing."). Dr. Romesberg testified that "even though the prior legal proceedings were focused on the '537 patent," "the reasoning of these ten judges appl[ies] to all of the asserted patents in this case." 1021:4-7. In contrast, BGI's expert Dr. Metzker did not "opine whether there was any mistake by the Patent Office of any of the IPRs in considering that theory of Zavgorodny taught an azido blocking group and SBS was known and you could combine the two was because that wasn't within the scope of [his] assignment." Trial Tr. 868:12-17.

With respect to the other objective indicia, the record is replete with evidence. For example, for long-felt but unmet need, in previously attempting to invalidate the claims, BGI argued that "[b]efore August 2002, nucleotide analog chemistry was a focus of significant scientific and commercial resources" "driven by immense market pressure." TX0984-031. Yet, despite the "increasing demands in the community for better sequencing systems" starting "in the early 1990s" (Trial Tr. 888:10-12), the evidence shows that there was no one else "working with the azidomethyl as a protecting group between the time Zavgorodny was published until the Bentley paper" in 2008. Trial Tr. 902:5-8. Despite several research groups working on the problem, none were able to solve the problem that the asserted patents solved. *See, e.g.*, Trial Tr. 1057:9-24; 897:24-899:3 (Dr. Metzker tried dozens of different blocking groups "in search of a new reversible terminator that could be used in the SBS method" in the "2002-2003" time period and did not identify azido as a candidate). As a further example, BGI's employee Dr. Snezana Drmanac testified in 2008 when Illumina's *Nature* article was published, "Illumina's azido technology caught everybody's eye." Trial Tr. 736:3-4.

As another example, there is a multitude of evidence that BGI copied Illumina's technology. After discovering that Illumina used azidomethyl as a blocking group for its SBS chemistry, BGI

[3] JTX0007 and JTX0051.

decided to use azidomethyl in its own commercial products. Trial Tr. 277:17-278:9 (Zebra project, launched in 2015, used azido blocked nucleotides). There is extensive documentary and testimonial evidence showing that BGI copied Illumina's patented azidomethyl technology to develop its SBS products, including for example:

- Chongjun Xu testified that it used Acme Biosciences to analyze Illumina's blocked nucleotides. 279:21-280:11. Acme Biosciences concluded that Illumina used azidomethyl as a blocking group. TX2539; Trial Tr. 310:7-311:4, 312:10-16.
- BGI performed mass spectrometry and fluorescent spectra analysis on Illumina's blocking nucleotides. TX0653; TX0659.
- Several entities knew and approved of the use of Illumina's reagents to develop BGI's sequencing chemistry. Trial Tr. 287:13-288:7.
- Chongjun Xu sent an email stating "since we want to mimic XY to make sure it works in version 1" of its sequencing chemistry" wherein "XY" refers to Illumina. TX0369; Trial Tr. 309:12-310:6.
- Chongjun Xu sent an email in 2015 summarizing the status of various components of BGI's sequencing chemistry. Under a section entitled "SE50 sequencing kit," the email states "We have 2 versions of reagent, one is BB, other (called Zebra) is developed from XY." TX0394-002.

In addition, Dr. Romesberg testified that the evidence demonstrates that BGI performed LCMS analysis on Illumina's nucleotides and copied the precise structure of Illumina's modified nucleotides disclosed in the 2008 Bentley paper that was published in *Nature*. Trial Tr. 632:7-9; 646:13-650:18.

Dr. Romesberg considered all of the objective ample evidence of objective and concluded that it supported his opinion that the patents were non-obviousness. *See, e.g.*, Trial Tr. 1056:6-24; 1056:25-1061:8 (summarizing some of the evidence supporting the objective indicia of non-obviousness). Similarly to the prior IPRs and Court cases, Dr. Metzker failed to provide any opinions on any of these objective indicia aside from commercial success, despite understanding that they were "part of the obviousness analysis." Trial Tr. 879:19-886:23; Dkt. No. 525-12 at 52:22-53:8, 53:18-23. The Federal Circuit has repeatedly confirmed that "evidence rising out of the so-called 'secondary considerations'

must always when present be considered en route to a determination of obviousness. Indeed, evidence of secondary considerations may often be the most probative and cogent evidence in the record." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Litig.*, 676 F.3d 1063, 1075–76 (Fed. Cir. 2012). Objective indicia must "be considered as part of all the evidence, not just when the decision-maker remains in doubt after reviewing the art." *Id.* Dr. Metzker's failure to even address this evidence, which the record at trial showed was abundant and persuasive, demonstrates that BGI has failed to meet its burden of proving by clear and convincing evidence that the Asserted Patents are invalid.

1. BGI Has Failed To Prove Claim 3 of the '444 Patent Is Invalid Because It Would Have Been Obvious To Modify Zavgorodny In Light Of Non-Sequencing Prior Art

BGI has not provided sufficient evidence that Claim 3 of the '444 Patent (or any of the Asserted Patents) are invalid as obvious by the combination of Zavgorodny and/or Kovacs, a reference that is wholly unrelated to sequencing, much less, the highly specific sequencing-by-synthesis. BGI's arguments regarding Zavgorodny alone and other uses for nucleosides likewise fail.

For example, the deficiencies in BGI's evidence, and the reason a POSITA would not have been motivated to combine Zavgorodny with Kovacs were summarized by Illumina's expert, Dr. Romesberg. Dr. Romesberg explained that Zavgorodny does not disclose the types of antivirals addressed in Kovacs, but rather is directed to a different class of antivirals which are a type of polymer. *See* Trial Tr. 1035:4-1036:18. As Dr. Romesberg explained, these molecules do not include phosphates, nucleotides, and are certainly not substrates for a DNA polymerase. *Id.* 1035:10-1036:12. On the other hand, Kovacs discussed some specific and potent nucleotides, which could serve as antivirals. Kovacs notes that these were worth further studies. *See id.* 1034:6-1035:3. As further evidence, Dr. Romesberg explained that predicting antiviral activity is particularly difficult, and changing one atom from the known antiviral AZT resulted in a loss of antiviral activity. *See* Trial Tr. 1038:12-1039:5. And given the difficulties in drug development, Dr. Romesberg notes that there are no antiviral drugs with 3'-O blocked nucleosides. *See* Trial Tr. 1039:9-1040:11.

Concurring with Dr. Romesberg, BGI's expert, Dr. Metzker testified that in the last three decades following the publication of Zavgorodny, there have been enormous efforts to develop antiviral therapies to address the AIDS epidemic. Notwithstanding these efforts, there are no published

experiments testing azidomethyl as a potential antiviral. *See* Trial Tr. 907:9-13; *see also id.* 908:5-9. Dr. Metzker also testified that he is unaware of any reversible terminators being used as an antiviral therapy. *See id.* 908:10-15. Dr. Metzker's limited testimony cannot provide clear and convincing evidence of obviousness. Instead, after three decades following the publication of Zavgorodny, and the concerted efforts to address the AIDS epidemic, the lack of published experiments testing azidomethyl as an antiviral is further evidence that the patent is not obvious.

Additionally, the record does not support a conclusion of obvious as to any of the other reasons Dr. Metzker articulated as to why a skilled artisan would modify the nucleoside disclosed in Zavgorodny to synthesis a nucleotide. Dr. Metzker's conclusory statement that a skilled artisan "would have immediately have done that without any thought whatsoever" does not meet the standard for motivation to combine. 810:15-16. For example, Dr. Romesberg testified that all of the proposed "motivations" Dr. Metzker provided are not supported by the literature. 1039:19-1040:15.

2. BGI Has Failed To Prove It Would Have Been Obvious To Modify Zavgorodny In Light Of Any Sequencing-by-Synthesis Prior Art

BGI did not meet its burden to prove that the Asserted Claims are invalid as obvious in light of either Zavgorodny reference and/or Greene and Wuts in light of Parce[4] or any other SBS art. As described above, the PTAB and several Courts have repeatedly concluded that it would not have been obvious to combine Zavgorodny with several SBS references. *See* § II.A. BGI has failed to provide evidence that the combinations of prior art it now asserts render the patents obvious. For example, BGI argued at trial that the Parce reference it now asserts does not require efficiency. 852:18-853:3. However, as one example, Dr. Metzker's own prior art paper describing SBS instructs that the nucleotides must be "deprotected efficiently" and that this is one of the "stringent requirements" that are "formidable obstacles. TX3258.001. As a further example, Dr. Romesberg testified that Parce does require efficiency, and a skilled artisan would know it is required of any SBS method. Trial Tr. 1043:24-1044:5, 1044:17-23, 1117:7-14. The remaining arguments Dr. Metzker makes are simply retreading past failed arguments that do not reach the clear and convincing threshold.

[4] TX3236.

3. BGI Has Failed To Prove The "Cleavable Linker" Claims Are Invalid As Obvious

BGI did not meet its burden to prove that the "cleavable linker" claims in the '025, '200, and '537 patents are invalid as obvious. The most Dr. Metzker did was assert that the use of a cleavable linker was "one of the standard methods that were used in the SBS methods" and generally made reference to the fact that Dower, Tsien, and Ju "describe[] using a cleavable linker." Trial Tr. at 862:4-11; *see also* 863:6-23 ("[T]he general use of linkers, which has been used since the 1980s, is to move the dye."). Dr. Metzker's conclusory statements that cleavable linkers were "standard methods" and cursory references to prior art do not satisfy Defendants' burden in proving invalidity.

In the first instance, Dr. Metzker provides no detail about the scope of the prior art as related to cleavable linkers. In fact, Dr. Metzker does not even identify where the references to cleavable linkers are in Dower, Tsien, and Ju, and none of those references have even been entered into evidence. Further, even if such vague assertions were sufficient to establish that elements of a patented invention were independently known in the prior art (which they don't), they are not enough to show by clear and convincing evidence that the claims are obvious. Notably, Dr. Metzker provides no explanation as to why a person of ordinary skill would be motivated to combine the cleavable linkers with the other elements of the patented invention. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) ("A patent composed of several elements is not proved obvious by merely demonstrating that each of its elements was, independently, known in the prior art.").

For example, in *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, the Federal Circuit upheld the district court's JMOL grant of no invalidity on the basis that the obviousness testimony of the defendant's expert was "conclusory and factually unsupported." 694 F.3d 1312, 1327-28 (Fed. Cir. 2012). There, Verizon's expert gave "essentially a conclusory statement that a person of ordinary skill in the art would have known . . . how to combine any of a number of references to achieve the claimed inventions." *Id.* at 1327. Such testimony, the Federal Circuit held, "is fraught with hindsight bias." *Id.* at 1327. In addition, such a generic analysis cannot provide a motivation to combine as it fails to explain "why a person of ordinary skill in the art would have combined specific elements from specific references *in the way the claimed invention does*." *Id.* at 1328 (emphasis in original).

Similarly here, Dr. Metzker's provides no analysis as to why a person of ordinary skill would

combine the cleavable linkers he asserts were known in the prior art with the other elements of the patented invention. Instead, like the expert in *ActiveVideo*, Dr. Metzker provides generic testimony about the availability of linkers, with no reference to "any specific combination of prior art elements." *Id.* As such, there is insufficient evidence on record for a reasonable jury to find that the "cleavable linker" claims are obvious.

4. BGI Has Failed To Prove The Remaining Dependent Claims Are Invalid As Obvious

The Asserted Claims include limitations beyond those BGI provided evidence for at trial. Because BGI has failed to provide any evidence those additional limitations are present in the prior art and there would be a motivation to combine any references that disclose them with a reasonable expectation of success, BGI has failed to show all of the Asserted Claims are invalid. For example, aside from addressing the motivation to combine a disclosure of an azidomethyl protecting group with an SBS method, the only further limitation BGI even attempted to address (doing so insufficiently, as described above) was the presence of a cleavable linker in the Asserted Claims of the '537, '200, and '025 Patents. Trial Tr. 861:24-863:3. Thus, BGI did not address at all the further limitations of at least claims 4 and 6 of the '537 Patent, claims 19 of the '200, and claims 9, 31, 33, 34, 42, 47, and 50 of the '025 Patent.

"Each claim of a patent ... shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim." *Cir. Check Inc. v. QXQ Inc.*, 795 F.3d 1331, 1337 (Fed. Cir. 2015) (quoting 35 U.S.C. § 282). Here, BGI has the burden of establishing that each Asserted Claim of the '025, '200, and '537 patents are invalid as obvious. *Id.* Therefore, even if BGI presented sufficient evidence of obviousness as related to the independent claims of the '025, '200, and '537 patents, it would be improper to invalidate the dependent claims "absent any evidence regarding the additional limitations of these claims." In addition, because unaddressed elements of the dependent claims are not "substantially materially identical" to the addressed elements of the independent claims, BGI cannot group all the asserted claims together to extend its obviousness analysis to the dependent claims. *Dayco Prod., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1370-71 (Fed. Cir. 2003). Therefore, because BGI did not present

evidence of obviousness as to the remaining elements of the dependent claims, no reasonable jury could find that those dependent claims were obvious.

B. BGI Has Failed To Prove The Asserted Claims Of The '973, '537, '200, and '025 Patents Are Invalid For Lack Of Enablement or Written Description

The Asserted Claims are sufficiently enabled and described and, thus, are not invalid. The evidence shows that BGI has failed to meet its clear and convincing burden. For example, with respect to enablement, Dr. Metzker failed to even address the *Wands*[5] factors. Additionally, Dr. Romesberg testified that "all of the asserted claims in this case" are "fully described" and "fully enabled." Trial Tr. 1064:15-17.

1. BGI Has Failed To Prove Claim 13 Of The '973 Patent Lacks Enablement Or Written Description Of "Unlabeled" Embodiments

BGI has failed to show that the embodiments which cover "monitoring the incorporation of complementary nucleotides without having a label" (Trial Tr. 856:7-11) lack enablement or written description. The evidence shows that the specification and the knowledge in the art provided the teaching to practice the claimed method without the use of labels, the specification described that detection could be performed by any suitable means and a working example showing detection without a label, and that the team of inventors contemplated such schemes. For example:

- Dr. Metzker admitted that Illumina's patents "[a]re very limited and narrow in their scope" because "because they're focused specifically on the azido blocking group" and "a person of ordinary skill in the art could perform sequencing by synthesis just by following the prior art." Dkt. No. 525-12 at 56:18-57:3; Trial Tr. 908:24-909:3.
- Dr. Metzker further admitted that it was known in the art how "an ordinary skilled artisan could perform sequencing by synthesis without a label." Trial Tr. 909:24-910:8.
- Dr. Romesberg testified that "'973 patent describe[s] and enable[s] both labeled and unlabeled embodiments without the need for undue experimentation" because, for example, a person of ordinary skill in the art would have "known how to choose the right type of detection method based upon whether the nucleotides were going to be added all together or one at a time." Trial Tr. 1067:6-1068:5.

[5] *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

- Dr. Romesberg further testified that the specification of the '973 Patent described that the detection could be done by "any suitable method" and "any conventional method, of which there were many [] known," (Trial Tr. 1067:21-25) and further shows "a working example of sequencing by synthesis" which does not use "the fluorophore for detection" and is thus shows that "unlabeled method of detection" "works." Trial Tr. 1068:21-1072:8.
- Dr. Balasubramanian testified that "the team [at Solexa] had a mixture of ideas" regarding labeling, including "methods that don't necessarily need four labels and could use combinations and ***even zero labeling***." Dkt. No. 525-13 at 311:6-312:4; *see also id.* at 312:5-313:9 ("… there was also ***the idea of not having a label*** that was discussed … there were ideas about different schemes that used less than four labels or some labels in combinations, and some of this also included ***the possibility of there being no label***.").

BGI has failed to meet its burden of proving Claim 13 of the '973 Patent is invalid for lack of enablement or written description.

2. BGI Has Failed To Prove That The Asserted Claims Of The '973, '537, '200, and '025 Patents Are Invalid For Lack Of Enablement or Written Description

BGI has failed to show that the Asserted Claims of the '973, '537, '200, and '025 Patents are invalid for lack of enablement or written description for any other reason. For example, Dr. Metzker opined that the removal conditions of the azidomethyl group are only summarily described in the '200 Patent, and that the azidomethyl structure is disclosed in Figure 3 as only one option of up to millions of blocking groups. Trial Tr. 844:23-847:17. These arguments are not supported by the evidence. For example, first, this argument cannot apply to the '973 Patent, which explicitly discloses both the synthesis and removal conditions of the claimed azidomethyl blocking group. *See, e.g.*, Trial Tr. 1062:6-10 ("Does the '973 patent show how to synthesize a 3 prime O azidomethyl molecule? A. It does." (discussing JTX038, '973 Patent at 47:21-31)), 1062:16-21 ("Q. Okay. And does the '973 patent describe and enable how to deblock that 3 prime O azidomethyl? A. Yes, it does" (discussing JTX038, '973 Patent at 59:47-52). Second, with respect to the shared specification of the '537, '200, and '025 Patents, for example, Dr. Romesberg testified that Figure 3 describes the azidomethyl blocking group

which would be "the one that would come to a chemist's mind." Trial Tr. 1063:10-24; *see also* JTX012, JTX083, and JTX084 at Figure 3. Additionally, Dr. Metzker's testimony that Figure 3 purports to include a large number of molecules is irrelevant to the enablement and written description requirement because his estimate includes non-azido molecules that are unclaimed. All of the Asserted Claims include one more limitations related to an azido blocking group. *See also* Trial Tr. 1064:4-14. Furthermore, as another example, the testimony of BGI's former expert, Dr. Sutherland, supports Dr. Romesberg's conclusions. Trial Tr. 1064:18-1065:23. As a further example, Dr. Metzker did not dispute that "one of ordinary skill in the art by at least 2002 knows all the facts and conditions that are necessary to successfully incorporate a 3-prime-O-azidomethyl into a blocked nucleotide acid molecule using a polymerase." Dkt. No. 525-12 at 229:13-20. Thus, the evidence does not support that it would require undue experimentation or that the specification fails to describe the full scope of the Asserted Claims of the '973, '537, '200, and '025 Patents.

3. BGI Has Failed To Prove The Asserted Claims Of The '025 Patent Are Invalid For Lack Of Enablement or Written Description

In addition to the arguments above, BGI has failed to prove by clear and convincing evidence that the Asserted Claims of the '025 Patents are invalid for lack of enablement or written description. The Asserted Claims of the '025 Patent claim a labeled azido molecule, not a method of sequencing. JTX012 at Claims 1, 9, 27, 31, 33, 34, 42, 47, and 50; *see also* 1019:19-25. For example, BGI has failed to provide evidence that it would require undue experimentation to make the claimed molecules, and as described above, the evidence shows that a skilled artisan would be capable of making the claimed molecules. *See also* 1064:18-1066:10 ("there's not a million molecules claimed in the patent; but … synthesizing one or a couple of related compounds from that vast broad scope would be within the scope of one of skill in the art."). As a further example, BGI has failed to provide evidence that the specification of the '025 Patent does not describe the claimed molecules. *See, e.g.*, Trial Tr. 1063:10-24; JTX012, JTX083, and JTX084 at Figure 3. BGI's arguments with respect to enabling the method of sequencing or removal of the protecting group are irrelevant to the Asserted Claims of the '025 Patent, and thus BGI has failed to meet its burden.

V. CONCLUSION

For the foregoing reasons and reasons Plaintiffs previously identified and submitted to the Court, Plaintiffs respectfully request that the Court issue an order that none of the Asserted Claims are invalid.

Date: November 22, 2021

Respectfully submitted,

/s/ Edward R. Reines

EDWARD R. REINES (Bar No. 135960)
DEREK C. WALTER (Bar No. 246322)
NATE NGEREBARA (Bar No. 317373)
MELINDA ROOT (Bar No. 334485)
WEIL, GOTSHAL & MANGES LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065
Tel: (650) 802-3000
Fax: (650) 802-3100
edward.reines@weil.com
derek.walter@weil.com
nate.ngerebara@weil.com
melinda.root@weil.com

DOUGLAS W. MCCLELLAN (*pro hac vice*)
MELISSA L. HOTZE (*pro hac vice*)
WEIL, GOTSHAL & MANGES LLP
700 Louisiana, Ste. 1700
Houston, TX 77002
Telephone: (713) 546-5000
Facsimile: (713) 224-9511
doug.mcclellan@weil.com
melissa.hotze@weil.com

ANDREW P. GESIOR (*pro hac vice*)
WEIL, GOTSHAL & MANGES LLP
767 Fifth Avenue
New York, NY 10153
Telephone: (212) 310-8000
Facsimile: (212) 310-8007
andrew.gesior@weil.com

AUDRA SAWYER (Bar No. 324684)
WEIL, GOTSHAL & MANGES LLP
2001 M Street NW, Suite 600
Washington, DC 20036
Telephone: (202) 682-7274
audra.sawyer@weil.com

Attorneys for Plaintiffs
ILLUMINA, INC. AND ILLUMINA CAMBRIDGE LTD.